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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,509	06/28/2001	Hiroaki Shizuya	CIT1390-1	8122
28213	7590	12/17/2002		
GARY CARY WARE & FRIENDENRICH LLP 4365 EXECUTIVE DRIVE SUITE 1600 SAN DIEGO, CA 92121-2189			EXAMINER	MARVICH, MARIA
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 12/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/896,509	SHIZUYA, HIROAKI
	Examiner Maria B Marvich, PhD	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 22 October 2002.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-12, 14-34, 36-55 is/are rejected.
- 7) Claim(s) 13 and 35 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 28 June 2001 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: _____.                                   |

## **DETAILED ACTION**

Claims 1-55 are pending in this application.

### ***Election/Restrictions***

Upon further consideration, the restriction requirement mailed 9/17/02 is withdrawn. All claimed embodiments will be examined.

### ***Specification***

The abstract of the disclosure is objected to because it uses the abbreviation BAC without defining it. Correction is required. See MPEP § 608.01(b).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 25-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Use of the phrase "a corresponding essential gene" in claims 25 and 55 and by dependency claims 26-42 is broad and indefinite. It is not clear to what "corresponding" refers.

Claims 46-48 recites the limitation "introduction of BAC into the host cell" in claim 43. There is insufficient antecedent basis for the term "the host cell". BAC is introduced into the test cell according to the claim.

Claims 2, 25 and 43 and by dependency 26-42 and 44-55 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such

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omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: how the gene is obtained by homology with the identified essential chromosomal gene in the test cell.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 14-34, 36-45, 47 and 49-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying essential gene in an test organism and screening bacterial genes in a pathogenic bacterium through the use of *E. coli* as a host cell, it does not provide an enabling disclosure for any host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Electronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

- 1) Unpredictability of the art. This invention recites a method for identifying an essential gene in a test organism or for screening bacterial genes in a pathogenic

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bacterium. The invention proposes, as a method for both, creating merodiploid cells through the introduction of a BAC comprised of a segment of DNA from a test organism or pathogenic bacterium. Said segment is homologous to the chromosomal DNA of a haploid test organism and the entire genomic sequence of the host organism must be known (page 10, line 16-18). Given the great number of bacteria and the corresponding greater number of genes encoded by the genome of each of these bacteria, the use of any host cell was not high art at the time of invention.

In addition to the need to know the DNA sequence for the entire host genome, the host cell must also perform a variety of functions such as the ability to be transformed and stably propagate the transformed DNA (Kim et al, applicant cited). Additionally, the host cell must be haploid while replicating, and be resistant to environmental conditions to which it will be subjected to prevent BAC replication. Therefore, the use of any host cell renders the invention unpredictable unless the host is characterized according to these characteristics.

2) State of the art. As stated in Shizuya and Mehr (Keio J of Medicine, 2001, applicant cited), the BAC system was designed based upon *E.coli* due to the wealth of information in its genetics and molecular biology (page 27, line 11-13). *E.coli* is commonly used for a variety of technical aspects of the invention such as transformation and are transformable by a variety of methods such as electroporation, transduction and transfection. Specific strains used for this include DH5 $\alpha$ .

The state of the art of the identification of essential genes in prokaryotes has primarily focused on the use of antisense inhibitors to inhibit the activity of essential genes.

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3) Number of working examples. The specification provides by way of example, two examples in which *E.coli* is utilized as the host cell.

4) Amount of guidance provided by applicants. For guidance on the host cell, we are told "for convenience, therefore the host cell is preferably a prokaryotic cell whose entire genome has been mapped so that the location of each gene therein is known" (page 10, line 16-18). Specifically, in the invention, the *E. coli RecBC-SbcBC* host strain is used as it encourages double recombination events rather than reciprocal Campbell type recombination events resulting in "allelic replacement".

5) Nature of invention. The invention recites a method for the identification of genes utilizing a BAC cloning system. The invention relies on the disciplines of molecular biology and prokaryotic cell culture.

6) Level of skill in the art. The level of skill in the art covering this invention was high at the time of invention. A person of skill in the art would have the skills for the genetic manipulations of the invention as well as molecular cloning and characterization required for the invention.

7) Scope of the invention. This invention has narrow scope in that it recites a method for identifying essential genes in haploid organisms.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue experimentation and excessive experimentation in order to practice the claimed invention.

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Claims 1-12, 14-34, 36-45, 47 and 49-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants claim methods of identifying an essential chromosomal gene or screening bacterial genes in haploid organisms. Said methods employ a genus of haploid host cells.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. In the instant case, applicants disclose that *E. coli*, *Salmonella* and *B. subtilis* could be used as host cells in the invention. Provided for by example in the invention is *E. coli* (*RecBC-SbcBC* as a specific example). Given the diversity of and the uncertainty of, the identity of any host cell whose genome sequence is completely known must be empirically determined. In an unpredictable art, the disclosure of one example in one genus would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claims 1-12, 14-34 and 36-55 are rejected.

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Claims 13 and 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Zeta Adams, whose telephone number is (703) 305-3291.

Maria B Marvich, PhD  
Examiner  
Art Unit 1636

December 13, 2002

DAVID GUZO  
PRIMARY EXAMINER  
